Desmosomes are intercellular junctions that tightly link adjacent cells. Desmoplakin, a cell adhesion and cytoskeleton protein encoded by the DSP gene, is an obligate component of functional desmosomes that anchors intermediate filaments to desmosomal plaques. The DSP gene contains 24 exons and spans around 45 kb genomic distance that was mapped to chromosome 6p24.3. Alternative splicing results in two distinct protein isoforms. Mutations in DSP gene cause familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 8 (ARVD/C8) and dilated cardiomyopathy with wooly hair and keratoderma. ARVD/C is an autosomal dominant disease characterized by partial degeneration of the myocardium of the right ventricle, electrical instability and sudden death. Dilated cardiomyopathy with woolly hair and keratoderma is characterized by dilation of the left ventricle with alterations in muscle contractility, wooly hair, keratotic skin conditions, and sometimes congestive heart failure and death. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for DSP mutations. Individuals are tested by DNA sequencing of the coding exons of the DSP gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

**REASONS FOR REFERRAL**

Molecular confirmation of familial arrhythmogenic right ventricular dysplasia/cardiomyopathy type 8 (ARVD/C8) and dilated cardiomyopathy with wooly hair and keratoderma.

**METHODOLOGY**

Genomic DNA is analyzed for DSP mutations by DNA sequencing of the coding exons of the DSP gene, as well as the exon/intron junctions and a portion of the 5' and 3' untranslated regions. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

**SERVICE FEES**

<table>
<thead>
<tr>
<th></th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$1500 per sample</td>
<td>81406</td>
</tr>
<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
</tr>
</tbody>
</table>

**SENSITIVITY**

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-24 of DSP.

**SPECIMEN REQUIREMENTS**

- **Blood (preferred):** EDTA (purple-top) tubes: *Adult:* 5 cc *Child:* 5 cc *Infant:* 2-3 cc
- **Tissue:** Frozen (preferred), RNAlater
- **Other Body Fluids and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire